

WHAT IS CLAIMED IS:

1. A method of identifying a new composition with a desired activity, the method comprising:

5 providing a first set of compositions, wherein at least one member of the first set of compositions comprises at least a first demonstrated activity and a second desired activity;

10 determining a genetic response profile for each member composition of the first set of compositions by a) providing a plurality of cell lines, wherein the plurality of cell lines comprises at least one modified cell line which differs from a corresponding parent cell line in either the first demonstrated activity or the second desired activity; b) treating each member of the plurality of cell lines with each member composition of the first set of compositions; and c) detecting one or more responses to the member composition;

15 comparing the one or more responses from the genetic response profile to the first demonstrated activity and second desired activity of each member composition, thereby identifying a pattern of responses correlating to a decrease in the first demonstrated activity and an increase in the second desired activity; and

20 screening a second set of compositions for the pattern of responses, thereby identifying a new composition with the desired activity.

2. The method of claim 1, wherein the modified cell line differs from the corresponding parent cell line in the activity or concentration of a selected protein or nucleic acid.

25 3. The method of claim 2, wherein the activity or concentration of a selected protein is altered in response to an addition of one or more agents to the parent cell line.

30 4. The method of claim 3, wherein the one or more agents comprise compositions that modify DNA structure, alter DNA activity, alter protein expression, inhibit protein functional activity, induce protein functional activity, or combinations thereof.

5. The method of claim 4, wherein the compositions that alter DNA activity or alter protein expression comprise transcription inducers, transcription

inhibitors, translation inducers, translation inhibitors, compositions that alter post-transcription modification, compositions that alter splicing, or compositions that alter transportation.

6. The method of claim 4, wherein the one or more agents comprise
5 one or more antisense agents, ribozymes, protein ligands, growth factors, antibodies, antigens, antibiotics, transcription inhibitors, transcription enhancers, translation inhibitors, or translation enhancers.

7. The method of claim 1, wherein providing the plurality of cell lines comprises performing a genetic selection.

10 8. The method of claim 1, wherein the at least one modified cell line comprises a cell line that is drug resistant.

9. The method of claim 1, wherein providing the set of compounds comprises providing one or more drug compositions identified as a treatment for the first demonstrated activity.

15 10. The method of claim 1, wherein the second desired activity comprises an antiproliferative activity.

11. The method of claim 1, wherein the second desired activity comprises an antineoplastic activity.

12. The method of claim 1, wherein the first or second set of
20 compositions comprises between about 5 and about 50 compositions.

13. The method of claim 1, wherein the first or second set of compositions comprises between about 10 and about 20 compositions.

14. The method of claim 1, wherein the first or second set of compositions comprises one or more compound analogs.

25 15. The method of claim 1, wherein providing the plurality of cell lines comprises providing cell lines derived from different types of tissues or tumors, primary cell lines, genetically-modified cell lines, or combinations thereof.

16. The method of claim 1, wherein providing the plurality of cell lines comprises providing target-specific modified cell lines and parent cell lines.

30 17. The method of claim 1, wherein the plurality of cell lines comprises about two to about ten cell lines.

18. The method of claim 1, wherein the plurality of cell lines comprises cell lines optimized for the analysis of a particular disease area of interest.

19. The method of claim 18, wherein the particular disease area of interest comprises cancer, inflammation, cardiovascular disease, diabetes, an infectious disease, a proliferative disease, an immune system disorder, or a central nervous system disorder.

5 20. The method of claim 1, wherein one or more cell lines of the plurality of cell lines are selected from the group consisting of: PC3, DU145, LNCaP, MDA-PCa 2a, MDA-PCa 2b, ARCaP, 293, 293Tet-Off, CHO-AA8 Tet-Off, MCF7, MCF7 Tet-Off, LNCap, T-5, BSC-1, BHK-21, Phinx-A, 3T3, HeLa, PC3, DU145, ZR 75-1, HS 578-T, DBT, Bos, CV1, L-2, RK13, HTTA, HepG2, BHK-Jurkat, Daudi, 10 RAMOS, KG-1, K562, U937, HSB-2, HL-60, MDAHB231, C2C12, HTB-26, HTB-129, HPIC5, A-431, CRL-1573, 3T3L1, Cama-1, J774A.1, HeLa 229, PT-67, Cos7, OST7, HeLa-S, THP-1, and NXA.

15 21. The method of claim 1, wherein treating each member of the plurality of cell lines comprises administering varying concentrations of the plurality of compounds, thereby generating a dose-response.

22. The method of claim 1, wherein detecting the one or more responses comprises performing one or more broad scanning techniques and measuring the concentration or activity of at least one gene or gene product in the plurality of cell lines.

20 23. The method of claim 22, wherein the gene product comprises RNA and the one or more broad scanning techniques comprise microarray analysis, differential display, EST screening, or combinations thereof.

24. The method of claim 22, wherein the gene product comprises protein and the one or more broad scanning techniques comprise 2D-gel electrophoresis, 25 LC mass spectrometry, immunoscreening techniques, or combinations thereof.

25 25. The method of claim 1, wherein detecting the one or more responses comprises detecting a change in cellular transcriptional activity, cellular translational activity, gene product activity, stability, abundance, compartmentalization, phenotypic endpoint or a combination thereof.

30 26. The method of claim 1, wherein detecting the one or more responses comprises performing an RNA transcription assay, a protein expression assay, a binding assay, a protein function assay, a phenotype-based cellular assay, a metabolic assay, a small molecule assay, an ionic flux assay, a reporter gene assay, a cell

proliferation assay, an apoptosis assay, a cell adhesion assay, a cell invasion assay, a calcium signaling assay, a cell cycling assay, a nitric oxide signaling assay, a receptor expression assay, a gene promoter reporter assay, or a combination thereof.

27. The method of claim 22, wherein the gene product comprises one or more proteins selected from the group: signaling proteins, regulatory proteins, pathway specific proteins, and receptor proteins.

28. The method of claim 1, wherein detecting the one or more responses comprises performing flow cytometry.

29. The method of claim 1, wherein detecting the one or more responses comprises performing mass spectrometry.

30. The method of claim 1, wherein comparing the one or more responses comprises performing a comparative analysis on the one or more responses, the first demonstrated activity and the second desired activity.

31. The method of claim 30, wherein performing a comparative analysis comprises generating a graphical representation of the one or more responses over a plurality of time points.

32. The method of claim 30, wherein performing a comparative analysis comprises performing one or more techniques selected from the group consisting of: clustering analysis, multivariate analysis, analysis in n-dimensional space, principle component analysis, and difference analysis.

33. The method of claim 1, wherein screening the second set of compositions comprises screening a library of compositions.

34. The method of claim 1, wherein screening the second set of compositions comprises determining a genetic response profile for one or more members 25 of the library of test compositions by:

treating each member of the plurality of cell lines with a member composition of the library of test compositions; and
detecting one or more responses to the member composition.

35. The method of claim 34, wherein the one or more responses 30 collected for the genetic response profiles of the second set of compositions comprises a subset of the responses collected for the genetic response profiles of the first set of compositions.

36. A method of identifying one or more organisms that are sensitive to treatment with a drug composition, the method comprising:

identifying a set of genetic response markers of a biochemical process or disease state for which the drug composition is used as treatment;

5 providing a plurality of cell lines, wherein the plurality of cell lines comprises at least one modified cell line that differs from a corresponding parent cell line in a sensitivity to the drug composition;

10 determining one or more genetic response profiles by a) treating each member of the plurality of cell lines with the drug composition; and b) monitoring the set of genetic response markers;

comparing the one or more genetic response profiles to clinical data for a first population of organisms, thereby identifying a pattern of responses correlating to sensitivity to treatment with the drug composition; and

15 generating additional genetic response profiles for members of a second population of organisms and screening the additional genetic response profiles for the pattern of responses correlating to sensitivity, thereby identifying one or more organisms that are sensitive to treatment with the drug composition.

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